The Time has come . . .

HARVEIAN ORATION 1937

SIR ARTHUR HURST

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THE HARVEIAN ORATION

DELIVERED BEFORE
THE ROYAL COLLEGE OF PHYSICIANS OF LONDON
ON ST. LUKE'S DAY, 1937

BY

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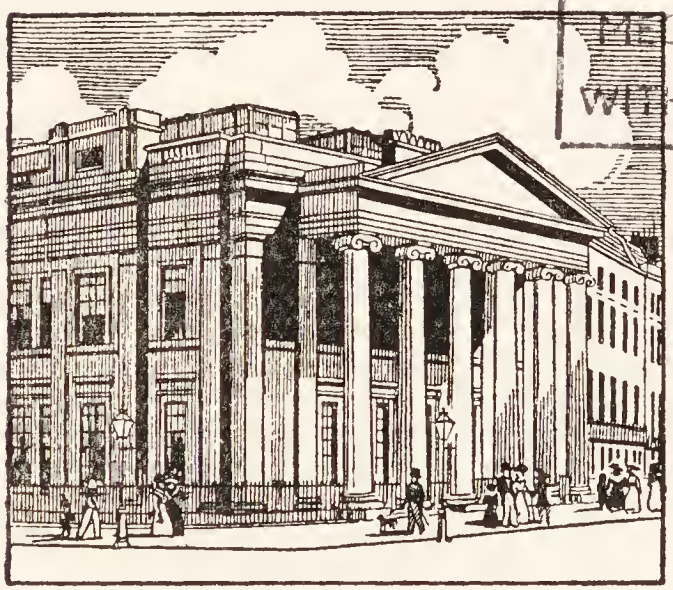

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THE TIME HAS COME . . .

The task of the two hundred and eighteenth Harveian Orator is not an easy one. It would indeed be almost impossible if he were still expected to follow to the letter the instructions laid down by Harvey when he conveyed his patrimonial estate of Burmarsh to the College for the endowment, among other objects, of an annual oration. It was natural that Harvey should desire that the oration should be delivered in Latin, for during the four years he spent as a medical student in Padua he acquired such a perfect colloquial knowledge of the language that he thought with equal facility in Latin and English, and the manuscript notes for his Lumleian lectures are written in a quaint mixture of the two languages. But happily in course of time more and more freedom of action has been permitted to the Orator. In the oration of 1863

Dr. Alexander Sutherland asked whether it would not be more convenient for the audience and easier for the orator to substitute English for Latin. The following year Dr. Robert Lee delivered the last oration in Latin; in 1865 Sir Henry Acland delivered the first in English. Since that date Harvey's injunction that the oration should be in Latin has no longer been obeyed, a mercy to those orators who, like myself, have forgotten most of the little Latin they ever knew, and perhaps a still greater mercy to the majority of their audience. In 1846 Dr. John Elliotson, rightly believing that he had something of real importance to say on the subject of "mesmerism", thought it necessary to take the unprecedented precaution of having a translation of his oration printed after the Latin original. So great was the general opposition to mesmerism at the time that the editor of the *Lancet* suggested that the portrait of Harvey should be turned with its face to the wall during the delivery of the oration.

I wonder how many Fellows of the College to-day would be capable of composing a Latin

oration which would have satisfied Sir Henry Halford, who was president when the College moved from its third home in Warwick Lane, near St. Paul's Churchyard, to its present quarters in 1825, and who was as famous for the ease and elegance with which he spoke Latin as for his skill as a physician. He was accustomed to compose Latin verse to beguile the tedium of driving in his carriage from one noble patient to another, and was so impressed with the importance of the "classical culture and staid philosophic habit of mind" engendered by education at the older universities that he strongly opposed the abolition of the rule that the fellowship should be confined to graduates of Oxford and Cambridge. It was not until 1835 that in spite of his continued opposition the reform was introduced.

BENEFACTORS

Harvey desired the Orator to commemorate "all the Benefactors of the College by name, and what in particular they have done for the benefit of the said College, with an exhortation to others to imitate those Benefactors." He would rejoice

that to-day our benefactors have become so numerous that this is no longer possible, for such a recitation, if brought up to date, would occupy the greater part of my time. I will therefore do no more than refer to certain recent benefactions of a novel character, which have an important bearing on the present and future activities of the College. Benefactors in the past have endowed lectureships to give Fellows an opportunity to describe the results of their original investigations and observations, and others have founded prizes to mark the accomplishment of good work done in various branches of medicine. But until recently the College had no means of encouraging young men of promise to follow Harvey's further instruction to seek every means of advancing the science of medicine by research. They were too often compelled to occupy much of their time with routine duties, which required no intellectual gifts and offered no sort of mental training, in order to earn a living. This deficiency has now been partly overcome by the munificence of the Leverhulme Trustees, James Maxwell Grant Prophit, Eliza Streatfeild, and Sir George

Mackenzie. It is gratifying to be able to record that the holders of the research scholarships founded by these benefactors have already done much admirable work. Four of them, Dr. J. F. Brock, Dr. S. J. Hartfall, Dr. R. L. Noble, and Dr. C. C. Ungley, have made important contributions to our knowledge of the subject which I propose to discuss to-day in connection with the modern application of the Harveian method of research.

RESEARCH

Harvey invited the Orator "to exhort the Fellows and Members of the College to search and study out the secrets of Nature by way of experiment". But he was equally alive to the importance of accurate observation. In *De Generatione* he notes how "many remarkable discoveries have been achieved by men who, following the traces of nature with their own eyes, pursued her through devious but most assured ways till they reached her in the citadel of truth. And truly in such pursuits it is sweet not merely to toil, but even to grow weary, when the pains of

discovery are amply compensated by the pleasures of discovery. . . . It were disgraceful, therefore, with this most spacious and admirable realm of nature before us, and when the reward often exceeds the promise, did we take the reports of others upon trust. . . . Nature is herself to be addressed ; the paths she shows us are to be boldly trodden ; for thus, and whilst we consult our proper senses,—shall we penetrate at length into the heart of her mystery."

HARVEY ON THE STOMACH

In 1642, whilst Harvey was in attendance on the King, a mob of citizen-soldiers entered his lodgings in Whitehall, stole all his furniture and scattered his papers, amongst which were the " Medical Observations " he had been collecting for many years and which he had intended to publish. Consequently much of what Harvey wrote is lost, and little is known about his interests in medicine beyond his two great works, *De Motu Cordis* and *De Generatione*. But there is a hint in the latter that he was a forerunner of Beaumont, Pavlov, Starling and Cannon, the pioneers of

gastro-intestinal physiology, as his observations on the digestion of birds contain without doubt the earliest recorded description of the motor functions of the stomach. " Almost all birds are provided ", he wrote, " with a double stomach ; one of which is the crop, the other the stomach, properly so called. In the former the food is stored and undergoes preparation, in the latter it is dissolved and converted into chyme. . . . In the crop the active grain that is swallowed is moistened, macerated, and softened, and then it is sent on to the stomach that it may there be crushed and comminuted. For this and almost all the feathered tribes swallow sand, pebbles, and other hard substances, which they preserve in their stomachs, nothing of the sort being found in the crop. Now the stomach in birds consists of two extremely thick and powerful muscles . . . so placed that, like a pair of millstones connected by means of hinges, they may grind and bruise the food ; the place of teeth, which birds want, being supplied by the stones they swallow. In this way is the food reduced and turned into chyme ; and then

by compression . . . the softer and more liquid part is forced out . . . and is transferred to the commencement of the intestinal canal. . . . The stones and other hard and rough substances which the birds have swallowed, if long retained, become so smooth and polished that they are unfit to comminute the food, when they are discharged. . . .

" If you apply the body of a hawk or an eagle, or other bird of prey, whilst fasting, to your ear, you will hear a distinct noise, occasioned by the rubbing, one against another, of the stones contained in the stomach." With the exception of a single reference to the subject by Hippocrates this is, I believe, the only record of an observation made by direct auscultation before 1800, when Bayle, whilst attending the lectures of Corvisart with Laënnec, examined the heart of a patient by applying his ear to the precordial region. The College possesses a reproduction of an imaginative painting of Harvey seated under a hedge reading a book whilst in charge of the Prince, afterwards Charles II, and the Duke of York during the battle of Edgehill. I would commend Harvey

with his ear applied to the body of a fasting eagle as a pleasing subject for a companion picture. Thirty years ago I obtained permission to repeat on a giraffe in the Zoo some observations I was making on the sounds heard on auscultation of the back and epigastrium during swallowing, as I thought that the length of its oesophagus would make their analysis less difficult. However, I had not Harvey's courage, and the experiment is still waiting to be made.

No further observations on the movements of the stomach were made in the two hundred years which followed the publication of *De Generatione*. Then in the course of his investigations on Alexis St. Martin's stomach Beaumont studied its movements, and in the latter half of the nineteenth century several physiologists investigated the movements and their nervous control in the exposed stomach of animals. But in 1897, when I went up to Oxford, the stomach was still portrayed in the text-books of anatomy as an enormous inert sac hanging across the middle of the abdomen. That same year a first-year Harvard medical student, W. B. Cannon, had the

inspiration to render the stomach of cats opaque to the rays recently discovered by Röntgen by adding bismuth salts to the food, a method which was soon to be applied to man as well as to cats, and was to open a new era in the investigation of the physiology and pathology of the stomach by visualising the gastric movements and so making it possible for every physician to be a Beaumont and every patient an Alexis St. Martin.

It is clear from the quotation I have given that Harvey regarded the stomach as the organ in which the food is diluted, softened and broken up in preparation for its absorption from the intestines. His work on the circulation of the blood had convinced him that the mesenteric veins convey nourishment from the intestines to the liver and thence by the vena cava to the heart, which distributes it to all parts of the body. It is curious, however, that in his old age he refused to accept Pecquet's convincing demonstration that the lacteals, which he had himself observed in the course of his dissections before Aselli had published the first description of them in 1622, were also concerned with the absorption of nourishment from the intestines.

Harvey's interest in physiology was thus not confined to the circulatory and generative organs, and his observations and experiments on the physiology of digestion were of fundamental importance. Instead of tracing the evolution of knowledge concerning the circulation since Harvey's time, as several of my predecessors have done, I propose to describe how the Harveian methods of combined observation and experiment have led to our present knowledge of the functions of the stomach.

WILLIAM HARVEY AND WILLIAM BEAUMONT

In the 52nd Exercise of *De Generatione* Harvey describes the case of a young nobleman, the apex of whose heart, covered by a suppurating membrane, was exposed as a result of an injury he had received as a child. In spite of this he was in excellent health and "felt adequate to any exercise or expedition". Harvey describes how he demonstrated to King Charles the movements of the young man's heart, and how in systole the apex emerged and protruded. "And his most excellent majesty, as well as myself, acknowledged

that the heart was without the sense of touch ; for the youth never knew when we touched his heart."

Two hundred years later Alexis St. Martin, a young Canadian trapper, received a gunshot wound in the abdomen. He came under the care of William Beaumont, a surgeon in the United States army, who took him into his own house and for two years nursed him back to health. The wound eventually healed, leaving a gastric fistula surrounded by a ring of prolapsed mucous membrane. Beaumont, who was endowed with the same spirit of enquiry as Harvey, engaged St. Martin as his servant, and for two periods between 1825 and 1833, amounting in all to twenty-four months, made almost daily observations and experiments, which laid the foundation of our knowledge of gastric digestion. Harvey's observations were concerned with the mechanical action of the stomach in altering the physical properties of the food so as to render it fit for absorption. Beaumont's work was concerned with the changes which occur in the stomach as a result of the digestive activity of the gastric juice.

He described the physical properties of gastric juice and had samples analysed, confirming Prout's recent discovery that it contained free hydrochloric acid. He showed that the juice is secreted only in response to the entry of food into the stomach and demonstrated its action on different kinds of food both within the body and *in vitro*. He recorded how as a result of fear and anger, febrile disturbances and excessive indulgence in alcohol the gastric mucous membrane became red and swollen and the juice was replaced by a secretion of mucus.

For twenty years after 1833 Beaumont made repeated attempts to persuade St. Martin to return to him so that he could continue his investigations, but without success. In 1840 the British Association made a grant of £200 with the object of bringing St. Martin to England so that further experiments on the physiology of digestion might be carried out on him in this country, but he refused to leave his Canadian home, where he died, aged 83, in 1880.

The next important step in the progress of knowledge concerning gastric digestion was the

employment of the stomach tube, which had long been used as a means of treating cases of poisoning. This was done by Leube in 1871, though the first " test-meal " had been given over a century before by Réaumur to his pet kite, which had the habit—like other kites—of rejecting from its stomach anything which it could not digest. In a paper on the digestion of birds read before the Académie des Sciences in 1752, twenty years after his invention of the thermometer which bears his name, he described how he fed his kite by giving food enclosed in small metal tubes, the ends of which were closed by a wire grating. The tubes were subsequently rejected and their contents examined. Meat was partly dissolved and showed no sign of putrefaction. Bone was also dissolved, but vegetable material remained unaltered. He then filled his tubes with pieces of sponge and obtained for the first time pure gastric juice, which he found turned blue paper red.

In 1885 Ewald and Boas invented the test-breakfast, and in 1915 Rehfuss, using Einhorn's duodenal tube, introduced the fractional test-meal. In 1920 the normal standard of secretory activity

was laid down by Izod Bennett and Ryle as a result of their examination of a hundred medical students. Since then many physicians, including several Fellows and Members of the College, have carried out physiological and clinical observations with the fractional test-meal, which have done much to elucidate the complicated problems concerned with the secretory activity of the stomach in health and disease.

THE ANTISEPTIC BARRIER OF THE STOMACH

As long ago as 1784 Spallanzani of Pavia demonstrated the antiseptic action of gastric juice by showing that it prevented and even arrested the putrefaction of meat. Thus meat moistened with gastric juice did not decompose, and the putrid odour of decomposing meat was lost on introducing it into the stomach of an animal. In recent years the subject has been reinvestigated by Knott, a Member of the College, who has shown that the normal sterility of the stomach and upper part of the small intestine depends upon the secretion of hydrochloric acid in the gastric juice. In achlorhydria the abnormally alkaline secretion

of the contents of the small intestine affords a favourable medium for the growth of the *Bacillus coli*, which invades not only the small intestine, but also the stomach. The infection of the duodenum is of special importance, as it often leads to an ascending infection of the bile ducts and is responsible for many cases of cholecystitis. The loss of the acid antiseptic barrier of the stomach also permits infection of the small intestine by swallowed organisms in streptococcal infections of the teeth and tonsils, and Camps has demonstrated the importance of the acid barrier as a protection against infection by typhoid, paratyphoid, dysentery and cholera germs. Utilisation of this knowledge should in the future do much to reduce the incidence of these infections amongst Europeans. A fractional test-meal should be an essential part of the examination of soldiers and civilians about to serve in the East, and the presence of achlorhydria, which would be discovered in about 4 per cent. of their number, should be regarded as an absolute bar against such service.

GASTRIC JUICE AND THE ABSORPTION OF IRON

Faber of Copenhagen showed in 1909 and again in 1913 that achlorhydria in women is often associated with simple anaemia. This simple achlorhydric anaemia has been very thoroughly investigated during the last few years, especially by Witts and subsequently by other Fellows and Members of the College. When normal gastric juice is secreted, the iron present in organic combination in the food is readily assimilated by the small intestine. In the absence of free hydrochloric acid deficient absorption of iron occurs. This leads to a simple microcytic anaemia if as a result of an ill-chosen diet the quantity of iron in the food is no greater than the minimal amount required by people with normal gastric juice, especially if excess of blood is lost owing to menorrhagia.

ADDISON'S ANAEMIA A DISEASE OF THE STOMACH

In 1880 Samuel Fenwick, a Fellow of the College, whose admirable work on the pathology of the stomach is apt to be forgotten to-day, noticed that the glandular structure of the gastric

mucous membrane of patients dying from Addison's anaemia was atrophied and contained so little pepsin that no *post mortem* digestion took place. He suggested that the lack of normal gastric juice which resulted from this atrophy must interfere with the formation of blood and that Addison's anaemia might consequently be regarded as a direct result of atrophy of the gastric glands. In the years which followed the constant association of Addison's anaemia with achlorhydria gradually became recognised, but Fenwick's theory was forgotten. The pioneer work of William Hunter on oral and intestinal sepsis led to the assumption that achlorhydria favoured the production of a haemolytic toxin in the intestines and that this was the cause of Addisonian anaemia. Against this theory, however, was the absence of any change in the blood in the large majority of people with achlorhydria, and gastric digestion was as completely in abeyance and bacterial growth in the stomach and duodenum was just as vigorous in uncomplicated achlorhydria as in achlorhydria with severe anaemia. Moreover, the administration of

hydrochloric acid failed to produce any striking improvement in most cases of Addison's anaemia. It seemed clear, therefore, that although achlorhydria was constantly present in Addison's anaemia, it was not directly responsible for its development.

This was the state of our knowledge on the subject when, in 1931, Castle, a young Harvard physician, who had been working with Minot on the treatment of Addison's anaemia with liver, solved the problem in a manner which would have delighted the heart of Harvey. He first demonstrated that the administration of the gastric juice of a normal man had no more effect on the blood of a patient with Addison's anaemia than an artificial gastric juice consisting of hydrochloric acid and pepsin. He then made the remarkable observation that a mixture of meat with gastric juice was as effective as liver in the treatment of the anaemia, but that this was not a result of peptic digestion, as the gastric juice could not be replaced by hydrochloric acid and pepsin, and the mixture was most effective when the hydrochloric acid was completely neutralised so as to prevent the

occurrence of peptic activity. It is now known that the gastric juice contains an intrinsic factor, haemopoietin, which reacts with an extrinsic factor present in meat and in other foods to produce an active principle ; this is stored in the liver and passes as required to the bone marrow, the normal activity of which depends upon its presence. In the absence of this principle the embryonic blood-forming tissue fails to reach maturity and the characteristic blood picture of Addison's anaemia results.

The history of human physiology since the time of Harvey contains few more fascinating examples than this of the solution of an apparently insoluble problem by inductive reasoning and experiment.

NEUROPOIETIN

In 1922 an Australian Fellow of the College, J. R. Bell, and I found that achlorhydria is constantly present in subacute combined degeneration of the spinal cord and that in untreated cases an Addisonian type of anaemia almost invariably develops before death. It was at first thought

that Minot's discovery of the liver treatment of Addison's anaemia was not applicable to the associated nervous disorder, but Ungley and Suzman, the former a Leverhulme Scholar, and the latter a Member of the College, have shown that when the dosage is adequate the disease can not only be arrested, but great improvement and sometimes complete recovery may be expected to occur. As Addison's anaemia and subacute combined degeneration of the cord rarely develop with equal rapidity in the same patient, and in many cases either may be present alone for long periods with no symptom or sign of the other, it seems clear that they must be caused by deficiency in different, though closely associated substances. Further evidence of this is afforded by the fact that the gastric juice of patients with achlorhydria and subacute combined degeneration of the spinal cord but normal blood can be shown to contain haemopoietin by its curative influence on Addison's anaemia. I have suggested that the gastric juice contains an additional ferment, to which the name neuropoietin may be given. This is the intrinsic factor which forms with an extrinsic

factor in the food an active principle that is stored in the liver and is required for the normal nutrition of the central nervous system. Its deficiency results in subacute combined degeneration of the spinal cord. The gastric juice thus has the surprising function of supplying a substance essential for the nutrition of the central nervous system.

It is now known that the proximal half of the stomach secretes hydrochloric acid and pepsin and that the distal half secretes an alkaline juice containing haemopoietin and neuropoietin (Meulengracht). Hydrochloric acid is the first to disappear, then pepsin, and finally haemopoietin and neuropoietin.

The stomach is thus an organ of extraordinary versatility. It protects the intestines from chemical and mechanical insults by diluting, softening and breaking up the food, it digests protein and curdles milk, it offers an antiseptic barrier to bacteria from above and below, and it produces substances which are essential factors in the production of the active principles required for the blood-forming activity of the bone marrow and for the nutrition of the central nervous system.

In recent years surgery has offered abundant opportunities for studying the physiology of the stomach in man by means of operations which have often made experiments on animals superfluous. Investigations after gastric operations, most of which have been carried out by Fellows and Members of this College in co-operation with Fellows of the College of Surgeons, have shown that in spite of its many functions the stomach is not an absolutely essential organ. Gastro-jejunostomy and, more frequently, gastrectomy may totally abolish gastric digestion by giving rise to achlorhydria, but in spite of this the stools contain no excess of undigested food, and the loss of the protection against mechanical and chemical irritation and of the acid antiseptic barrier of the gastric juice manifests itself by a tendency to diarrhoea in only a small proportion of cases. Simple achlorhydric anaemia is, however, a common sequel of partial gastrectomy, but Addison's anaemia is surprisingly rare and does not even develop in every case of total gastrectomy. This is now known to be due to the fact that the

mucous membrane of the first part of the duodenum, the glands of which are similar in structure to those of the pyloric end of the stomach, secretes a juice containing haemopoietin, the quantity of which is sufficient in most people to compensate for the absence of gastric juice.

The interest shown by Harvey and his friend and patron, King Charles the First, in the absence of sensibility of the heart would have been extended to the observations which it is now possible to make on individuals whose stomachs have been completely removed by operation. Twenty-six years ago in my Goulstonian Lectures I showed that the mucous membrane of the alimentary tract from the pharyngo-oesophageal sphincter to the junction of the rectum with the anal canal is insensitive not only to tactile, but also to thermal stimuli, and that the only adequate stimulus to sensation in the stomach and intestines is distension, with the exception of the warm epigastric sensation produced by the introduction of strong alcoholic drinks into the stomach. After complete removal of the stomach a patient does not spontaneously appreciate his loss by the absence

of any familiar sensation. Appetite and the general sensations associated with hunger are unaffected, and on swallowing nothing unusual is noticed unless the patient takes his food too rapidly, when he feels some fullness in the epigastrium, but he cannot distinguish this from what he would have felt under similar conditions before his operation, although presumably it is caused by distension of the part of the jejunum anastomosed with the oesophagus. Close observation, however, shows that the feeling of emptiness after long abstention from food is not felt, and the patient does not experience the pleasant glow in the epigastrium which should follow the drinking of neat spirits or a liqueur.

In describing the development of our knowledge of the functions of the stomach I have mentioned only a few of the names of those to whom we are indebted for that knowledge. It will be observed that the majority of them, especially during the last thirty years, were hospital physicians. We see, therefore, that to-day there are still physicians engaged in the practice of medicine, who endeavour to follow in the

footsteps of Harvey and take an active part in advancing the science of physiology.

CLINICAL RESEARCH AND GASTRIC PATHOLOGY

The last thirty years, which have witnessed such a revolution in our knowledge of the functions of the stomach, have witnessed an equally great revolution in our knowledge of gastric disorders. When I was house-physician in 1905 the x-rays had not yet begun to throw light on gastro-intestinal problems. We occasionally gave a Boas-Ewald test-meal, but the information it yielded was of infinitely less value than that obtained from the modern fractional method. The significance of occult blood was unknown. Consequently diagnosis depended upon the history and physical examination alone. As the latter is completely negative in the large majority of gastric cases diagnosis depended almost entirely on the history. But the correlation of history with pathological findings was possible only in fatal cases, as the pathology of the living—the greatest gift of surgery to medicine—was still in its infancy. Consequently the diagnosis of the minor and

chronic disorders was a matter of guess-work, as there were no means of discovering the pathological cause of symptoms in non-fatal cases. But a former Harveian Orator, Sir William Hale-White, and the President of the College, Lord Dawson, were at that time showing that combined clinical and pathological research in the tradition of Bright, Addison and Wilks could still bring important facts to light, when they demonstrated that gastric ulcer was really a disease of middle life affecting males more frequently than females and not, as had hitherto been universally believed, a disease of anaemic young women. This discovery was soon to be confirmed by Moynihan, whose genius has been curiously under-estimated by his surgical colleagues, who, whilst acclaiming what he did for the Art of Surgery, forget what he did for the Science of Medicine. His discovery of the clinical picture of duodenal ulcer was as much a piece of original scientific research as the discovery of a new element or a new star, and as equally deserving of recognition. It is, perhaps, difficult for the present generation to realise that thirty years ago, when Moynihan was already

accurately diagnosing duodenal ulcer from the clinical history almost daily in Leeds, it had never been diagnosed in London apart from an occasional lucky guess in cases of perforation and of melaena, and his papers on the subject were regarded as the products of a too vivid imagination. Duodenal ulcer was diagnosed in the absence of haemorrhage for the first time at Guy's in May 1907, and its frequency was not recognised on the Continent till nearly twelve years later. In 1913, Ewald, one of the leading German gastro-enterologists of the time, stated his belief that only one duodenal ulcer occurred for every forty-five gastric ulcers.

THE PATHOGENESIS OF CARCINOMA OF THE STOMACH

It is now generally believed that carcinoma never develops in a healthy stomach. There is abundant evidence to show that in the 70 per cent. of cases with achlorhydria the carcinoma results from malignant degeneration of chronically inflamed mucosa, the achlorhydria being a result of the preceding gastritis and not of the carcinoma. In the remaining 30 per cent. of cases with a

normal or high acidity the evidence is equally conclusive that the carcinoma is a result of malignant degeneration of a simple ulcer. The chronic gastritis and the simple ulcer are caused by chronic irritation, the former especially in individuals born with a hyposthenic gastric constitution and the latter in those with a hypersthenic gastric constitution.

The irritants which give rise to gastritis and gastric ulcer are mechanical, chemical and thermal ; food, insufficiently broken up and softened owing to its coarse character, to hurried meals, or to insufficient teeth or dentures, irritates the mucous membrane mechanically ; alcohol and tobacco, highly seasoned food, drugs, and saliva swallowed by patients with oral sepsis are chemical irritants ; very hot and very cold food and drinks are thermal irritants.

The total incidence of cancer is approximately the same in both sexes, in the rich and the poor, and in all nations. If cancer of the uterus and breast are excluded, the relative incidence in different organs is the same in men and women. It is also the same in the rich and the poor and in

different nations, with one supremely important exception—the stomach being involved three times as often in the poor as in the well-to-do, and in only 22 per cent. of all cases of cancer in men in Great Britain compared with 42 per cent. in America, 55 to 60 per cent. in Holland, Bavaria, Norway, Sweden and Spain, and 66 per cent. in Czechoslovakia.

We have recently tried to discover the cause of the difference between the incidence in Great Britain and Holland—22 compared with 55 per cent. The total incidence of cancer is the same in the two countries, and we have found, as might be expected, that the incidence of the hyposthenic and hypersthenic stomach is also the same. We must therefore look for a difference in the extrinsic causes. Herbert and Bruske have compared the teeth and dietetic habits of 500 out-patients at Guy's Hospital with those of 500 at the Wilhelmina Gasthuis in Amsterdam : 58 per cent. of the Dutch ate too quickly and chewed insufficiently compared with 11 per cent. of the English ; gross oral sepsis was present in 44 per cent. of the Dutch and 28 per cent. of the English.

Spiced foods were eaten in excess by 48 per cent. of the Dutch and 19 per cent. of the English, and official statistics show that the consumption of spirits is much higher in Holland than in England ; 43 per cent. of the Dutch were accustomed to swallow their food and drink at a temperature over 60°, compared with only 22 per cent. English. Lastly, 62 per cent. of the Dutch, but only 13 per cent. of the English smoked more than 4 ounces of tobacco, whether cigarettes, pipes or cigars, a week, and 18 per cent. of the Dutch, but none of the English, chewed tobacco.

It is surely significant that wherever there is a difference between the dental condition and the dietetic and smoking habits in England and Holland it is to the advantage of England. It seems reasonable to assume that the more frequent and more severe irritation of the gastric mucosa in the Dutch leads to a greater incidence of achlorhydric gastritis in individuals with the hyposthenic gastric constitution and of gastric ulcer in those with the hypersthenic gastric constitution. If our views as to the origin of carcinoma of the stomach are correct, this would

explain why its incidence is so much greater in Holland than in Great Britain. Insufficient teeth and dentures, and oral sepsis, coarser food and stronger tobacco may account for the greater incidence in the poor compared with the rich.

At present we have no knowledge of how the general liability to cancer can be controlled, and the organ inferiority which predisposes to achlorhydric gastritis on the one hand, and to gastric ulcer on the other, cannot be modified. But the extrinsic causes—gastric irritants of all kinds—however trivial they may appear to be, can be avoided, and it should at least be possible to lower the incidence in the very poor by two-thirds to bring it down to the level of the incidence in the well-to-do. By preventing the development of achlorhydric gastritis and gastric ulcer in the predisposed by simple hygienic methods cancer too should be prevented ; and even if gastritis and gastric ulcer are not abolished, their early recognition and adequate treatment should result in their cure before malignant degeneration has had time to occur.

The fractional test-meal has made it possible to investigate the secretory functions of the stomach with considerable accuracy, and the x-rays afford a means of studying its motor functions and the deformities produced by disease. But so long as the mucous membrane of the stomach remained inaccessible to visual inspection there could be little advance in our knowledge of gastritis, which is now known to be much the most common of all gastric disorders. The invention of a flexible gastroscope by Schindler in 1932 may therefore be regarded as a landmark in the study of the stomach in health and disease, which ranks in importance with that of the cystoscope in the study of the bladder. I am glad that in this country the gastroscope has not suffered the fate of the cystoscope and come to be regarded as a surgical instrument. Several of our younger Fellows and Members are already expert in its use, and their investigations are adding greatly to our knowledge of the pathology of the stomach. If one thinks for a moment how little could be known of glossitis or pharyngitis without inspection

of the tongue or pharynx, it is easy to realise how much our knowledge of gastritis must gain from gastroscopy. The interpretation of radiographs of the stomach is being revolutionised, and for some purposes, such as the investigation of post-operative gastric disorders and of the healing of gastric ulcers under treatment, gastroscopy will in the future take the place of radiology.

MEDICAL FRIENDSHIP

Harvey desired that the Fellows of the College should live in brotherly love and affection. This is best promoted by frequent opportunities of meeting, such as are offered by the four annual dinners of the Fellows' Club, which was founded in 1872 to succeed the still older Comitia Dining Club. I am happy that the feast which Harvey desired should be "kept within the College" on the day of the Oration "for all Fellows that shall please to come", and towards the cost of which he made on the occasion of the first dinner an endowment of fifteen pounds, is to be revived to-night, as it gives an additional stimulus to good fellowship among Fellows of different generations.

Until thirty years ago provincial Fellows too often had to work in most undesirable isolation. This is now a thing of the past, largely owing to the good work of the Association of British Physicians, the foundation in which in 1907 we owe to seven former Harveian Orators—Osler, Herringham, Garrod, Rose Bradford, Rolleston, Hale-White and Robert Hutchison. The Association also gives London physicians an opportunity of seeing the hospitals and laboratories of other University cities in Great Britain and Ireland, but it is still a blot on London medicine that there is so little inter-communication between the staff and students of the twelve teaching hospitals, in striking contrast with the conditions in the University of Paris, where students are free to attend clinics and lectures in any hospital they please. Visitors from the Dominions and America generally know more about the methods of teaching and the day to day work of the London hospitals than the hospital physicians themselves, who are satisfied to continue their activities in a far from splendid isolation. Occasional visits of a physician with his firm to a friend at another

hospital is good for both physician and student, as I can testify from my own experience in the last few years, and I hope that this practice will become increasingly common.

The international relations of the College have in the past been very limited. On rare occasions distinguished physicians from abroad have lectured in this room, and during the tercentenary celebrations of the publication of *De Motu Cordis* two of the representatives of the learned societies of the world, Pavlov and Wenckebach, were elected Honorary Fellows.

In company with a group of Fellows of the College I have in each of the past nine years made a pilgrimage to some foreign medical centre. We have been greatly impressed by the kindness with which we have always been received, and by the eagerness that our hosts have shown in demonstrating the work in which they were interested, and in hearing about medical research and medical education in Great Britain.

A direct result of the international co-operation which can follow such meetings is seen in a

paper in the April number of the *Quarterly Journal of Medicine*, which would never have seen the light had it not been for the 1936 meeting of the Medical Pilgrims. In this paper Donald Hunter, Snapper and Groen of Amsterdam, and Witts describe a new syndrome of hypogonadism, alopecia, depression of metabolism, microcytic or macrocytic anaemia, subacute combined degeneration of the cord and achlorhydria. They suggest that the syndrome is the result of a lesion of the anterior lobe of the pituitary gland, which must, it is assumed, produce under normal conditions a stimulant to the secretion of haemopoietin. How greatly Harvey would have appreciated an investigation of this kind is clear from a letter he wrote to John Vlackveld of Haarlem six weeks before his death. "Nature is nowhere accustomed more openly to display her secret mysteries than in cases where she shows traces of her workings apart from the beaten path; nor is there any better way to advance the proper practice of medicine than to give our minds to the discovery of the usual law of nature, by the careful investigation of cases of rarer forms of disease."

I should like to suggest that we might follow the example of our sister College and the Académie de Chirurgie of Paris by exchanging visits with the Académie de Médecine. Might we not also renew our old associations with the Medical Schools of Padua and Leyden, where so many of our seventeenth and eighteenth century Fellows received the greater part of their medical education, and with the American College of Physicians, whose Fellowship is open to Canadians as well as to citizens of the United States? We might in these and similar ways do something to extend Harvey's admonition to live in brotherly love and affection beyond the confines of the College to physicians in other parts of the world, and so add our small, though by no means negligible, contribution towards the maintenance of peace by the promotion of international friendship.

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On St. Luke's Day, October 18th, 1602, the youthful Harvey must have listened to the Oration in Praise of Medicine, which every year opened the medical session in the University of Padua.

I like to think that since his death, fifty-five years later, his spirit makes an annual pilgrimage to this College on St. Luke's Day to listen to the Oration which he founded. He would regret the decay of classical education which has led to its delivery in English instead of Latin, but he would, I think, find no other sign of backsliding. Though modest in life, his vanity would be flattered by the efforts of a whole series of learned Orators to bring to light everything which can add to our meagre knowledge of his life and character and of the friends among whom he worked. He would, I feel sure, have been particularly gratified by Dr. Robert Hutchison's clear demonstration that he was endowed with the priceless gift of a sense of humour.

He would have noted with surprise that the Presidential chair is occupied this afternoon for the seventh year in succession by the same Fellow, an event with only a single precedent since Sir Henry Halford ruled over the College for the twenty-four years between 1820 and 1844. He would realise that this could only be the result of the immense satisfaction of the Fellows for the

manner in which its affairs have been conducted by Lord Dawson, during whose tenure of office the influence of the College on medical education, medical research and the public health has become more profound and more far-reaching than ever before.

Harvey would be pleased to see how well his admonitions have been remembered, and to find that after three hundred years Fellows and Members of the College are still taking a leading part in " the research and study of the secrets of Nature by way of experiment ". And at the end of each Oration he would return to the Elysean fields, happy in the knowledge that " to the honour of the profession " the Fellows of the College continue " to live in mutual love and affection amongst themselves ".